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**Eph-Pak2a signaling regulates branching of the pharyngeal endoderm by inhibiting late-stage epithelial dynamics.**

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**Public Summary:**

In this publication, Choe et al investigate how changes in tissue shape are coordinated to build the vertebrate head. By live imaging a type of endodermal tissue in developing zebrafish, they uncovered a critical role for "Eph" and Pak" proteins in bending tissue sheets to generate the folds of the mouth cavity.

**Scientific Abstract:**

Branching morphogenesis depends on the precise temporal and spatial control of epithelial dynamics. In the vertebrate head, endodermal branches, called pharyngeal pouches, form through the transient stratification, collective migration and reorganization of epithelial cells into bilayers. Here, we report novel requirements for the EphrinB ligands B2a and B3b, the Ephb4a receptor and the Pak2a kinase in the development of pouches and the posterior facial skeleton that depends on pouches for its segmentation. Time-lapse imaging in zebrafish shows that EphB-Pak2a signaling is required to stabilize pouch epithelial cells at the end of branching morphogenesis. Transgenic rescue experiments further demonstrate that endodermal Eph-ephrin signaling promotes pouch integrity by targeting Pak2a to the plasma membrane, where subsequent activation by Wnt4a-Cdc42 signaling increases junctional E-cadherin in maturing pouches. Integration of Eph-ephrin and Wnt4a signaling through Pak2a thus signals the end of branching morphogenesis by increasing intercellular adhesion that blocks further epithelial rearrangements.

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